

AN 10536865 IFIPAT;IFIUDB;IFICDB
 TITLE: EXO-S-MECAMYLAMINE FORMULATION AND USE IN TREATMENT
 INVENTOR(S): Newman; Mary, Valrico, FL, US
 Sanberg; Paul, Spring Hills, FL, US
 Shytle; Douglas, Lutz, FL, US
 Silver; Archie A., Tampa, FL, US
 PATENT ASSIGNEE(S): University of South Florida, US
 AGENT: Carl B. Massey, Jr. Womble Carlyle Sandridge & Rice,
 PLLC, Post Office Box 7037, Atlanta, GA, 30357-0037,
 US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2004044083	A1	20040304
APPLICATION INFORMATION:	US 2003-441947		20030923

	APPLN. NUMBER	DATE	GRANTED PATENT NO. OR STATUS
CONTINUATION OF:	US 2001-882935	20010615	
CONTINUATION-IN-PART OF:	WO 1999-US30153	19991216	

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 1998-112534P	19981216 (Provisional)
FAMILY INFORMATION:	US 2004044083	20040304
DOCUMENT TYPE:	Utility	

Patent Application - First Publication

FILE SEGMENT: CHEMICAL
APPLICATION

NUMBER OF CLAIMS: 20 7 Figure(s).

DESCRIPTION OF FIGURES:

FIG. 1 is a gas chromatograph printout showing that exo-Smecamylamine elutes purely at 63.971 minutes after placement on the column.
 FIG. 2 shows the structures of mecamlamine generally (+/-).
 FIG. 3 is a bar graph showing total distance traveled in 60 minutes by rats having undergone seven days of sensitization with saline or mecamlamine at one of 3 doses. The dagger symbol indicates significant differences from the Saline/Saline control group. The asterisk identifies significant differences from the Saline/Nicotine control group.
 FIG. 4 is a bar graph showing the center distance traveled by rats in the same study.
 FIG. 5 is a bar graph showing the vertical activity of rats in the same study.
 FIGS. 6A-6D are bar graphs showing the percentage of rats that seized (6A), latency to **seizure** (6B), duration of **seizure** (6C), and severity of seizures in rats treated with saline or various doses of mecamlamine and its stereoisomers followed by nicotine (3.6 mg/kg).
 FIG. 7 is a bar graph illustrating the mean total distance traveled in centimeters in rats receiving any of saline or 10 mg/kg mecamlamine or its stereoisomer.

AB . . . are treated by administering a therapeutically effective amount of exo-S-mecamylamine or a pharmaceutically acceptable salt thereof, substantially free of its **exo-R-mecamylamine**, said amount being sufficient to ameliorate the medical condition. The medical conditions include but are not limited to substance addiction. . . opiate, other psychostimulant and a combination thereof), aiding smoking cessation, treating weight gain associated with smoking cessation, hypertension, hypertensive crisis, **Tourette's** Syndrome and other tremors, cancer (such as small cell lung cancer), atherogenic profile, neuropsychiatric disorders (such as **bipolar** disorder, depressoin, an **anxiety** disorder, **schizophrenia**, a **seizure** disorder, **Parkinson** 's disease and **attention deficit** hyperactivity disorder), chronic fatigue syndrome, Crohn's disease, autonomic dysreflexia, and spasmogenic intestinal disorders.

GI . . . of rats in the same study.

FIGS. 6A-6D are bar graphs showing the percentage of rats that seized (6A), latency to **seizure** (6B), duration of **seizure** (6C), and severity of seizures in rats treated with saline or various doses of mecamylamine and its stereoisomers followed by. . .

ACLM 5. The pharmaceutical composition of claim 1 wherein the substantially pure **exo-S-mecamylamine** is greater than 95% by weight and **exo-R-mecamylamine** is less than 5% by weight.

6. The pharmaceutical composition of claim 1 wherein the substantially pure **exo-S-mecamylamine** is greater than 98% by weight and **exo-R-mecamylamine** is less than 2% by weight.

7. The pharmaceutical composition of claim 1 wherein the substantially pure **exo-S-mecamylamine** is greater than 99% by weight and **exo-R-mecamylamine** is less than 1% by weight.

8. The pharmaceutical composition of claim 1 wherein the substantially pure **exo-s-mecamylamine** is greater than 99.5% by weight and **exo-R-mecamylamine** is less than 0.5% by weight.

9. The pharmaceutical composition of claim 1 wherein the substantially pure **exo-S-mecamylamine** is greater than 99.7% by weight and **exo-R-mecamylamine** is less than 0.3% by weight.

. . . said method comprising administering a therapeutically effective amount of **exo-S-mecamylamine** or a pharmaceutically acceptable salt thereof, substantially free of its **exo-R-mecamylamine**, said amount being sufficient to alleviate cravings.

12. A method of treating **Tourette's Syndrome** in a human in need thereof, the method comprising administering to the human with **Tourette's Syndrome**, a therapeutically effective amount of **exo-S-mecamylamine** or a pharmaceutically acceptable salt thereof, substantially free of **exo-R-mecamylamine**, the amount being sufficient to decrease the signs and symptoms of **Tourette's Syndrome**.

. . . the human in need thereof, a therapeutically effective amount of **exo-S-mecamylamine** or a pharmaceutically acceptable salt thereof, substantially free of **exo-R-mecamylamine**, the amount being sufficient to decrease the signs and symptoms of the neuropsychiatric disorder.

17. The method of claim 16 wherein the neuropsychiatric disorder is **bipolar disorder, depression, anxiety disorder, panic disorder, schizophrenia, seizure disorders, Parkinson's disease and attention deficit hyperactivity disorder**.

L10 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:107915 CAPLUS

DOCUMENT NUMBER: 136:156476

TITLE: Exo-S-mecamylamine formulation for therapeutic uses

INVENTOR(S): Shytte, Douglas; Sanberg, Paul; Newman, Mary; Silver, Archie A.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of Appl. No. PCT/US99/30153.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002016371	A1	20020207	US 2001-882935	20010615
WO 2000035279	A1	20000622	WO 1999-US30153	19991216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

US 2004044083 A1 20040304 US 2003-441947 20030923
PRIORITY APPLN. INFO.: US 1998-112534P P 19981216
WO 1999-US30153 A2 19991216
US 2001-882935 A1 20010615

AB A pharmaceutical composition, suitable for administration by i.v., transdermal, intrathecal, oral, i.m., and bolus injection route, comprises substantially pure **exo-S-mecamylamine** or its salt, with <5% of **exo-R-mecamylamine**. The amount of **exo-S-mecamylamine** in the composition is about 0.5-1000 mg. The composition is useful for the treatment of medical conditions that include but are not limited to substance addiction (involving nicotine, cocaine, alc., amphetamine, opiate, or other psychostimulants), aiding smoking cessation, treating weight gain associated with smoking cessation, hypertension, tremors, cancer, atherogenic profile, neuropsychiatric disorders, chronic fatigue syndrome, Crohn's disease, autonomic dysreflexia, and spasmogenic intestinal disorders. For example, mecamylamine and its stereoisomers potently block nicotine-induced seizures in rats, with **exo-S-mecamylamine** displaying an overall higher therapeutic index over **exo-R-mecamylamine**.

IT Brain, disease
(Gilles de la **Tourette** syndrome; compns. containing **exo-S-mecamylamine** for treatment of drug dependence and other disorders)

IT Mental disorder
(**attention deficit** hyperactivity disorder; compns. containing **exo-S-mecamylamine** for treatment of drug dependence and other disorders)

IT Mental disorder
(**bipolar** disorder; compns. containing **exo-S-mecamylamine** for treatment of drug dependence and other disorders)

IT Alcoholism
Anticonvulsants
Antidepressants
Antihypertensives
Antiobesity agents
Antiparkinsonian agents
Antipsychotics
Antitumor agents
Antiviral agents
Anxiolytics
Drug dependence
Muscle relaxants
Nicotinic antagonists
Schizophrenia
Tremor

(compns. containing **exo-S-mecamylamine** for treatment of drug dependence and other disorders)

IT 107538-06-7P 107596-31-6P
RL: ADV (Adverse effect, including toxicity); BYP (Byproduct); PAC (Pharmacological activity); BIOL (Biological study); PREP (Preparation)
(compns. containing **exo-S-mecamylamine** free of **exo-R-mecamylamine**)

L10 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:107914 CAPLUS

DOCUMENT NUMBER: 136:156475

TITLE: **Exo-R-mecamylamine**

formulations for therapeutic uses
INVENTOR(S): Shytle, Douglas; Sanberg, Paul; Newman, Mary; Silver, Archie A.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of Appl. No. PCT/US99/30137.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002016370	A1	20020207	US 2001-882934	20010615
WO 2000035280	A1	20000622	WO 1999-US30137	19991216

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-112534P P 19981216
WO 1999-US30137 A2 19991216

TI **Exo-R-mecamylamine** formulations for therapeutic uses

AB A pharmaceutical composition, suitable for administration by i.v., transdermal, intrathecal, oral, i.m., and bolus injection route, comprises substantially pure **exo-R-mecamylamine** or its salt, with <5% of **exo-S-mecamylamine**. The amount of **exo-R-mecamylamine** in the composition is about 0.5-1000 mg. The composition is useful for the treatment of medical conditions that include but are not limited to substance addiction (involving nicotine, cocaine, alc., amphetamine, opiate, or other psychostimulants), aiding smoking cessation, treating weight gain associated with smoking cessation, hypertension, tremors, cancer, atherogenic profile, neuropsychiatric disorders, chronic fatigue syndrome, Crohn's disease, autonomic dysreflexia, and spasmogenic intestinal disorders. For example, pretreatment with mecamylamine and its stereoisomers of rats exposed to nicotine dose-dependently prevented the development of the sensitized locomotor responses to nicotine. Chronic exposure to mecamylamine actually reduced the locomotor response to nicotine to levels below that seen in the saline (control) group. Although both isomers of mecamylamine followed the same general pattern, **exo-R-mecamylamine** was generally more effective at lower doses, for center distance and vertical activity.

IT Intestine, disease
(Crohn's; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Brain, disease
(Gilles de la Tourette syndrome; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Antiarteriosclerotics
(antiatherosclerotics; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Mental disorder
(attention deficit hyperactivity disorder; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Mental disorder
(bipolar disorder; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
(capsules, soft; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
(capsules; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Tobacco smoke
(cessation; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Fatigue, biological
(chronic fatigue syndrome; compns. containing **exo-R-**

mecamylamine for treatment of drug dependence and other disorders)

IT Alcoholism
 Anticonvulsants
 Antidepressants
 Antihypertensives
 Antiobesity agents
 Antiparkinsonian agents
 Antipsychotics
 Antitumor agents
 Antiviral agents
 Anxiolytics
 Drug dependence
 Muscle relaxants
 Nicotinic antagonists
Schizophrenia
 Tremor
 (compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Opioids
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Catecholamines, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Nicotinic receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Human
 (compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders in humans)

IT Psychostimulants
 (dependence to; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
 (injections, bolus; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
 (injections, i.m.; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
 (injections, i.v.; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Spinal cord, disease
 (injury, autonomic dysreflexia; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
 (liqs.; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
 (oral; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
 (solids; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Intestine, disease
 (spasmogenic disorder; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)

IT Drug delivery systems
 (sustained-release; compns. containing **exo-R-**

mecamylamine for treatment of drug dependence and other disorders)
IT Drug delivery systems
(tablets; compns. containing **exo-R-mecamylamine**
for treatment of drug dependence and other disorders)
IT Drug delivery systems
(transdermal; compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)
IT 50-36-2, Cocaine 54-11-5, Nicotine 64-17-5, Ethanol, biological studies 300-62-9, Amphetamine
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)
IT 107538-06-7 107596-31-6
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)
IT 51-41-2, Norepinephrine 51-43-4, Epinephrine 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compns. containing **exo-R-mecamylamine** for treatment of drug dependence and other disorders)
IT 107538-05-6P 107596-30-5P
RL: ADV (Adverse effect, including toxicity); BYP (Byproduct); PAC (Pharmacological activity); BIOL (Biological study); PREP (Preparation)
(compns. containing **exo-R-mecamylamine** free of **exo-S-mecamylamine**)

L10 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 2000:420906 CAPLUS

DOCUMENT NUMBER: 133:53722

TITLE: **Exo-R-mecamylamine**
formulation and use in treatment

INVENTOR(S): Shytte, Douglas; Sanberg, Paul; Newman, Mary; Silver, Archie

PATENT ASSIGNEE(S): University of South Florida, USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035280	A1	20000622	WO 1999-US30137	19991216
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1139744	A1	20011010	EP 1999-967396	19991216
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002532393	T2	20021002	JP 2000-587609	19991216
US 2002016370	A1	20020207	US 2001-882934	20010615
PRIORITY APPLN. INFO.:			US 1998-112534P P	19981216
			WO 1999-US30137 W	19991216

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI **Exo-R-mecamylamine** formulation and use in treatment

AB A pharmaceutical composition includes a therapeutically effective amount of **exo-R-mecamylamine** or a pharmaceutically acceptable salt thereof, substantially free of **exo-S-mecamylamine**, in combination with a pharmaceutically acceptable carrier. Preferably the amount is about 0.5 mg to about 20 mg. Medical conditions are treated by administering a therapeutically effective amount of **exo-R-mecamylamine**, or a pharmaceutically acceptable salt thereof, substantially free of its **exo-S-mecamylamine**, said amount being sufficient to ameliorate the medical condition. The medical conditions include but are not limited to substance addiction (involving nicotine, cocaine, alc., amphetamine, opiate, other psychostimulant and a combination thereof), aiding smoking cessation, treating weight gain associated with smoking cessation, hypertension, hypertensive crisis, **Tourette's** Syndrome and other tremors, cancer (such as small cell lung cancer), atherogenic profile, neuropsychiatric disorders (such as **bipolar** disorder, **depression**, an **anxiety** disorder, **schizophrenia**, a **seizure** disorders, **Parkinson's** disease and **attention deficit** hyperactivity disorder), chronic fatigue syndrome, Crohn's disease, autonomic dysreflexia, and spasmogenic intestinal disorders.

ST mecamylamine isomer pharmaceutical therapeutic; drug addiction treatment mecamylamine isomer; wt gain smoking cessation mecamylamine isomer; hypertension **Tourette** syndrome cancer mecamylamine isomer; cardiovascular neuropsychiatric gastrointestinal disease mecamylamine isomer

IT Intestine, disease
(Crohn's; **exo-R-mecamylamine** formulation and therapeutic use)

IT Brain, disease
(Gilles de la **Tourette** syndrome; **exo-R-mecamylamine** formulation and therapeutic use)

IT Antiarteriosclerotics
(antiatherosclerotics; **exo-R-mecamylamine** formulation and therapeutic use)

IT Mental disorder
(**attention deficit** hyperactivity disorder; **exo-R-mecamylamine** formulation and therapeutic use)

IT Disease, animal
(autonomic dysreflexia; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
(bolus, injections; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
(capsules; **exo-R-mecamylamine** formulation and therapeutic use)

IT Nervous system
(catalepsy; **exo-R-mecamylamine** formulation and therapeutic use)

IT Fatigue, biological
(chronic fatigue syndrome; **exo-R-mecamylamine** formulation and therapeutic use)

IT Alcoholism

Antidepressants

Antihypertensives

Antiparkinsonian agents

Antipsychotics

Antitumor agents

Anxiolytics

Drug delivery systems

Drug dependence

Mental disorder

Movement disorders

Nervous system agents

Psychostimulants

Schizophrenia

Seizures

Tobacco smoke

(**exo-R-mecamylamine** formulation and therapeutic use)

IT Opioids
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (**exo-R-mecamylamine** formulation and therapeutic use)

IT Nicotinic receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (**exo-R-mecamylamine** formulation and therapeutic use)

IT Drugs
 (gastrointestinal; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
 (gelcaps; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
 (injections, i.v.; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
 (intrathecal; **exo-R-mecamylamine** formulation and therapeutic use)

IT Antitumor agents
 (lung small-cell carcinoma; **exo-R-mecamylamine** formulation and therapeutic use)

IT Mental disorder
 (manic bipolar disorder; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
 (oral; **exo-R-mecamylamine** formulation and therapeutic use)

IT Lung, neoplasm
 Lung, neoplasm
 (small-cell carcinoma, inhibitors; **exo-R-mecamylamine** formulation and therapeutic use)

IT Body weight
 (smoking cessation-associated weight gain; **exo-R-mecamylamine** formulation and therapeutic use)

IT Behavior
 (smoking; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
 (solids; **exo-R-mecamylamine** formulation and therapeutic use)

IT Intestine, disease
 (spasmogenic; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
 (sustained-release; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
 (tablets; **exo-R-mecamylamine** formulation and therapeutic use)

IT Drug delivery systems
 (transdermal; **exo-R-mecamylamine** formulation and therapeutic use)

IT 50-36-2, Cocaine 54-11-5, Nicotine 64-17-5, Ethanol, biological studies 300-62-9, Amphetamine
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (**exo-R-mecamylamine** formulation and therapeutic use)

IT 60-40-2, Mecamylamine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**exo-R-mecamylamine** formulation and
therapeutic use)

IT 107596-30-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**exo-R-mecamylamine** formulation and
therapeutic use)

IT 107538-05-6 107538-06-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**exo-R-mecamylamine** formulation and
therapeutic use)

L10 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2000:420905 CAPLUS

DOCUMENT NUMBER: 133:53721

TITLE: Exo-S-mecamylamine formulation and use in treatment

INVENTOR(S): Shytle, Douglas; Sanberg, Paul; Newman, Mary; Silver, Archie

PATENT ASSIGNEE(S): University of South Florida, USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035279	A1	20000622	WO 1999-US30153	19991216
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1139743	A1	20011010	EP 1999-967401	19991216
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002532392	T2	20021002	JP 2000-587608	19991216
US 2002016371	A1	20020207	US 2001-882935	20010615
US 2004044083	A1	20040304	US 2003-441947	20030923

PRIORITY APPLN. INFO.:
US 1998-112534P P 19981216
WO 1999-US30153 W 19991216
US 2001-882935 A1 20010615

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A pharmaceutical composition includes a therapeutically effective amount of
exo-S-mecamylamine or a pharmaceutically acceptable salt thereof,
substantially free of **exo-R-mecamylamine**, in
combination with a pharmaceutically acceptable carrier. Preferably the
amount is about 0.5 mg to about 20 mg. Medical conditions are treated by
administering a therapeutically effective amount of exo-S-mecamylamine, or a
pharmaceutically acceptable salt thereof, substantially free of
exo-R-mecamylamine, the amount being sufficient
to ameliorate the medical condition. The medical conditions include but
are not limited to substance addiction (involving nicotine, cocaine, alc.,
amphetamine, opiate, other psychostimulant and a combination thereof),
aiding smoking cessation, treating weight gain associated with smoking
cessation, hypertension, hypertensive crisis, **Tourette's**
Syndrome and other tremors, cancer (such as small cell lung cancer),
atherogenic profile, neuropsychiatric disorders (such as **bipolar**
disorder, **depression**, an **anxiety** disorder,
schizophrenia, a **seizure** disorder, **Parkinson's**

disease and **attention deficit** hyperactivity disorder), chronic fatigue syndrome, Crohn's disease, autonomic dysreflexia, and spasmogenic intestinal disorders.

ST mecamylamine isomer pharmaceutical therapeutic; drug addiction treatment mecamylamine isomer; wt gain smoking cessation mecamylamine isomer; hypertension **Tourette** syndrome cancer mecamylamine isomer; cardiovascular neuropsychiatric gastrointestinal disease mecamylamine isomer

IT Brain, disease
(Gilles de la **Tourette** syndrome; exo-S-mecamylamine formulation and therapeutic use)

IT Mental disorder
(**attention deficit** hyperactivity disorder; exo-S-mecamylamine formulation and therapeutic use)

IT Alcoholism
Antidepressants
Antihypertensives
Antiparkinsonian agents
Antipsychotics
Antitumor agents
Anxiolytics
Drug delivery systems
Drug dependence
Mental disorder
Movement disorders
Nervous system agents
Psychostimulants
Schizophrenia
Seizures
Tobacco smoke
(exo-S-mecamylamine formulation and therapeutic use)

IT Mental disorder
(manic **bipolar** disorder; exo-S-mecamylamine formulation and therapeutic use)

=> d'his

(FILE 'HOME' ENTERED AT 15:58:00 ON 30 APR 2004)

FILE 'STNGUIDE' ENTERED AT 15:58:05 ON 30 APR 2004

FILE 'HOME' ENTERED AT 15:58:09 ON 30 APR 2004

FILE 'REGISTRY' ENTERED AT 15:58:28 ON 30 APR 2004

L1 0 S EXO R MECAMYLAMINE/CN
L2 0 S EXO R MECAMYLAMNE
L3 7 S MECAMYLAMINE
L4 0 S EXO R MECAMYLAMINE
L5 0 S R MECAMYLAMINE

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DISSABS, DGENE, DRUGB, DRUGMONOG2, IMSDRUGNEWS, DRUGU, EMBAL, EMBASE, ESBIODBASE, IFIPAT, IMSPRODUCT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, ...' ENTERED AT 16:00:58 ON 30 APR 2004

L6 11382 S L3 OR EXO R MECAMYLAMINE
L7 14 S EXO R MECAMYLAMINE
L8 3387575 S TOURETTE? OR BIPOLAR OR DEPRESSION OR ANXIETY OR SCHIZOPHREN?
L9 12 S L7 AND L8
L10 5 DUP REM L9 (7 DUPLICATES REMOVED)